BONE REPLACEMENT MATERIAL COMPRISING CRYSTALLINE AND X-RAY AMORPHOUS PHASES

BACKGROUND OF THE INVENTION

Field of the Invention

[0001] The present invention relates to an X-ray amorphous-crystalline material with high solubility which can be used both as a bioactive bone replacement material, e.g. in the form of a coating applied onto metallic prosthesis sticks by thermal spraying or by rf sputtering, and as a substrate material in biotechnology, especially in tissue engineering, e.g. in the form of a ceramic sheet or of a compact or porous, i.e. spongiosa-like, scaffold-like, moulded body. The invention also relates to a manufacturing method.

Description of the Related Art

[0002] In principle, inorganic materials which are easily resorbed are known. Materials which are specifically used as bioactive bone replacement materials and dissolve quickly have also been described in the relevant literature. For example, there have been numerous publications dedicated to the successful clinical use of ceramic materials the main crystal phases of which are alpha- or beta-tricalcium phosphate (TCP). In addition, there have been comparative analyses of these two TCP phases using animal tests. It is known from EP 237043 that granulated materials made of alpha-TCP contain dicalcium phosphate on their surface, whose solubility was higher than that of the pure alpha-PCT core material, especially in the initial phase following an implantation.

[0003] The chemical solubility of the aforesaid granulated materials was surpassed by other bioactive materials based on calcium phosphates which in addition contain oxides of potassium, sodium, magnesium and/or silicon (EP 541564 B1) and the glassy-crystalline material of which is based on the following main crystal phases: Phase X, rhenanite, phase according to Ando (Phase A) and/or mixed crystals derived from the aforesaid phases.

SUMMARY OF THE INVENTION

[0004] The object of the invention is to provide an X-ray amorphous-crystalline material which enables a substantially direct joining of bones without connective tissue and/or the ex vivo cultivation of bone cells, and which dissolves in contact with bone tissue, and which at the same time has high solubilities which are adjustable in a more precise manner and, in the case of composite materials, coefficients of expansion adapted to certain steels. Another object of the invention is to develop a method for manufacturing the aforesaid material as well as manufacturing aids.

[0005] According to the invention, the bone replacement material consists of crystalline and X-ray amorphous phases and contains:

according to ^{31}P-NMR measurements, Q_0-groups of orthophosphate and Q_1-groups of diphosphate, the orthophosphates or Q_0-groups making up 70 to 99.9% by weight relative to the total phosphorus content of the finished material and the diphosphates or Q_1-groups making up 0.1 to 30% by weight relative to the total phosphorus content of the finished material, and

wherein according to X-ray diffractometric measurements and relative to the total weight of the finished material, 30 to 99.9% by weight of a main crystal phase consisting of $Ca_2K_{1-x}Na_{1+x}(PO_4)_2$, where $x = 0.1$ to 0.9, is contained and 0.1 to 20% by weight of a substance selected from the group consisting of $Na_2CaP_2O_7$, $K_2CaP_2O_7$, $Ca_2P_2O_7$ and mixtures thereof is contained as a secondary crystal phase, and

wherein the X-ray amorphous phases contained besides the main crystal phase jointly make up 0.1 to 70% by weight relative to the total weight of the finished material.

[0006] The secondary crystal phase is preferably made up of diphosphates, but one or more of the substances $NaPO_3$, KPO_3 and mixtures thereof can also be contained, the chain phosphates $NaPO_3$ and KPO_3 being detectable as Q_2-groups according to ^{31}P-NMR measurements. The chain phosphates are contained in an amount ranging between 0.1 and 10% by weight, preferably 0.1 and 4% by weight.

[0007] Further, the secondary phase may contain a silicate phase in an amount ranging up to 6% by weight, corresponding to the SiO_2 content.

[0008] The aforesaid main crystal phase and the constituents of the secondary crystal phase may contain magnesium in an amount ranging up to 10% by weight, calculated as MgO and relative to the weight of the finished material.

[0009] The orthophosphate phase represented by Q_0-groups preferably makes up 75 to 99% by weight, particularly 78 to 95% by weight.

[00010] The diphosphate phase represented by Q_1-groups preferably makes up 1 to 22% by weight, particularly 5 to 16% by weight.

[00011] The composition of the X-ray amorphous-crystalline material with high solubility which is based on CaO, P_2O_5, Na_2O, K_2O, MgO and optionally SiO_2 ranges between (in % by weight):

30	and 55	P_2O_5;	5	and 50	CaO;
1	and 20	Na_2O;	0.5	and 20	K_2O;
0	and 13	MgO;	0	and 10	SiO_2;

MgO or SiO_2 or a mixture thereof making up at least 1% by weight.

[00012] A preferred X-ray amorphous-crystalline material is composed as follows (in % by weight): 35 to 48 P_2O_5, 28 to 38 CaO, 2.5 to 15 Na_2O, 1.5 to 18 K_2O, 0.1 to 4 MgO, 0.0 to 3 SiO_2. A special preferred embodiment contains 40 to 52 P_2O_5, 28 to 33 CaO, 8.5 to 13 Na_2O, 9.5 to 15 K_2O, 1.5 to 3 MgO, 0.1 to 4 SiO_2.

[00013] In general, the term "X-ray amorphous-crystalline" material used herein cannot be clearly defined. "X-ray amorphous" as used herein refers to a material whose structure cannot be determined using standard XRD (X-ray diffractometry). The undetectable areas can be very small organized areas (micro-crystalline) as well as statistically unorganized areas. Unlike XRD, the ^{31}P-NMR results can be used to detect

the existence of any crystalline phase. Therefore quantitative estimates based on NMR and XRD results can be rather different. In the present case, this phenomenon seems to be particularly true of the diphosphate and chain phosphate contents; as a rule, ^{31}P-NMR measurements yield considerably higher contents than XRD. In some cases, no contents at all are found using XRD. This impressively shows why ^{31}P-NMR measurements are an essential prerequisite for characterizing and finally manufacturing the materials according to the invention. XRD measuring was made with PW 1710, Philipps, NL (CuK radiation).

[00014] Both crystalline and X-ray amorphous phases can therefore be provided in a thoroughly mixed state. It is of no importance for the present invention whether one phase is located adjacent to the other or one phase encloses the other. The term "main crystal phase" as used herein refers to a crystalline phase which is detected using X-ray diffraction and is contained in at least twice the amount of a secondary phase, concentrations of 20% and below, preferably below 15% by weight, being referred to as secondary phases.

[00015] For the sake of clarity, it must be pointed out that "$Ca_2KNa(PO_4)_2$" can certainly be identified as main crystal phase. However, there are shifts of intensity in the individual compositions, which may be rather substantial in some cases, due to the varying ratio of sodium to potassium or the inclusion of other ions (e.g. Mg^{2+} or SiO_4^{4-}) so that the formula "$Ca_2K_{1-x}Na_{1+x}(PO_4)_2$, where x = 0.1-0.9" is to be used. Higher Na contents are preferred, e.g. x = 0.2-0.9.

[00016] Surprisingly, solubility has been found to be particularly high if the product obtained by the melting process contains in particular crystalline diphosphates such as $Na_2CaP_2O_7$, $K_2CaP_2O_7$ and/or $Ca_2P_2O_7$ or even a majority of X-ray amorphous diphosphates besides the main crystal phases and X-ray amorphous orthophosphates. Further, it was surprisingly found that the aforesaid statement can be clearly quantified using ^{31}P-NMR measurements.

[00017] The ^{31}P-NMR measurements, which were carried out using a superconductive Fourier NMR spectrometer known as Avance DMX400 WB and manufactured by Bruker BioSpin GmbH (Germany), showed that the material consists of 70 to 99.9% by weight orthophosphate of calcium and in some cases orthophosphate of sodium, potassium and magnesium, wherein the aforesaid orthophosphate content is determined using ^{31}P-NMR measurements of Q_0-groups and refers to crystalline and/or X-ray amorphous material in its entirety. In addition, 0.1 to 30% by weight diphosphate of calcium and in some cases diphosphate of sodium, potassium and magnesium was found, wherein the aforesaid diphosphate content can be reliably determined using ^{31}P-NMR measurements (Q_1-groups) and refers to crystalline and/or X-ray amorphous material in its entirety.

[00018] Further, it is advantageous that 0.1 to 10% by weight chain phosphate consisting of sodium phosphate or potassium phosphate or both be contained, wherein this chain phosphate content represented by Q_2-groups is reliably determined by means of ^{31}P-NMR measurements and refers in particular to amorphous and, as the case may be, crystalline material in its entirety. In addition, 0.1 to 10% by weight of a silicate phase may be contained, depending upon the amount of SiO_2 added. Moreover, $Ca_5Na_2(PO_4)_4$ may be contained, although this is not preferred.

[00019] Further, it has surprisingly been found that the desired effect, i.e. a considerably improved solubility, is brought about by the presence of diphosphates and/or chain phosphates, preferably diphosphates, as will be demonstrated in Example 3.

[00020] The diphosphate contents result from a comparatively high phosphate content relative to the other constituents. The aforesaid phosphate content could also be the reason why the compositions according to the invention melt very easily yielding a rather fluid melt compared to known resorbable materials. Such a low-viscosity melt has the advantage that it has a better processability. That is the case for a frit of the melt or a direct blowing of the melt etc.

[00021] Further, it has surprisingly been found that due to the presence of diphosphates the ion discharge behaviour of the material (the X-ray amorphous-crystalline material), which in the beginning shows a strong alkaline reaction, changes more pronouncedly towards physiological pH values (7.4) than that of materials not containing diphosphate, provided the material was stored in deionized water. Due to this shift in pH values, the material is also of interest to biotechnology, in particular to tissue engineering.

[00022] The aforesaid feature can be enhanced by boiling a (compact or open-pore) moulded body in deionized water (37-90°C) thus leaching its surface so that the material or moulded body treated in this way has considerably lower pH values once the treatment is finished. This phenomenon could be put down to a reduction of the alkaline cations in the area near the surface of the material. The aforesaid process can be accelerated by boiling the material in a reactor, advantageously at a pressure of up to 10 bars. Such an embodiment of the invention is preferred.

[00023] It is an advantageous feature of the material according to the invention that its solubility can be adjusted within relatively wide ranges, depending upon the selected composition; specifically, the total solubility can range between 30 and 500µg/mg relative to the starting material if the test is carried out in 0.2M TRIS-HCl buffer solution at pH = 7.4, T = 37°C using a grain size fraction of 315-400µm, the duration of the test being 120h and the ratio of weighed-in sample to buffer solution being 50mg to 40ml.

[00024] The material according to the invention is manufactured by combining the substances suitable for preparing the mixture to be melted, their concentrations (relative to the total weight of the material) being in the range of 30-55% by weight CaO, 35-50% by weight P_2O_5, 1-20% by weight Na_2O, 0.5-20% by weight K_2O and 0.1-5% by weight MgO and optionally up to 5% by weight SiO_2, and melting them at between 1,550 and 1,650°C in a suitable crucible material, e.g. consisting of a Pt/Rh alloy, using multistage thermal treatment programmes including holding stages in the range between 200 and 1,500°C,

namely 1-2h at 350-400°C, 750-850°C and 950-1,050°C, e.g. 1h at 400, 800 and 1,000°C respectively. The melt is poured, preferably following a holding time of between 10 and 60min, and once the mass has solidified it is cooled down to room temperature in air (spontaneous cooling) or in a cooling furnace using a temperature-controlled cooling process, e.g. at a rate of 1 to 20 degrees/min, depending upon its intended use. The melt can also be blown thus directly forming the melt into spherical granules. In both cases, a spontaneous crystallization process takes place while the melt cools down. The mixture to be melted may comprise oxides, carbonates, hydrogen phosphates and/or ortho-phosphoric acid. The ^{31}P-NMR measurements yield different spectra allowing conclusions as to the raw materials used or indicating small amounts of iron oxides or manganese oxides contained therein. Preferred melting temperatures range between 1,590 and 1,650°C.

[00025] Once the material has cooled down, it is granulated and used as a bone replacement material, but it can e.g. also be ground, mixed with commonly used sintering aids and be isostatically pressed into moulded bodies in order to obtain a densely fired ceramic body after sintering. In general, the sintering temperatures range between 900 and 1,200°C.

[00026] Alternatively, the material manufactured according to the invention can e.g. be ground, mixed with commonly used sintering aids and processed into a slurry which is then applied onto a polyurethane sponge and sintered in several sintering stages at such high temperatures that the polyurethane sponge and the sintering aids are burnt completely and a spongiosa-like body is obtained the main crystalline constituents of which are $Ca_2K_{x-1}Na_{x+1}(PO_4)_2$ (x = 0.1-0.9) and $Na_2CaP_2O_7$, $K_2CaP_2O_7$, $Ca_2P_2O_7$ and/or mixed crystals in between these phases.

[00027] In a preferred embodiment of the invention, some of the raw materials used are melted separately in order to obtain a glass which acts as a sintering aid and can be used for the production of the spongiosa-like bodies in a particularly advantageous manner. The aforesaid glass is ground and can be added to the slurry

consisting of the material according to the invention which has been ground following the melting and cooling processes and then processed into a slurry. The glass melted separately can be added to the slurry in an amount ranging between 0.5 and 15, preferably 4-8% by weight, relative to the amount of solid matter contained therein, providing, however, that the individual components are not contained in the composition in larger amounts than those indicated in the invention. Such a glass can in particular be produced on the basis of SiO_2, MgO and Na_2O.

[00028] In this embodiment, the sintering process leads to a very solid structure of the moulded body, whereas parts of the moulded body may crumble away if all components are melted together and then sintered. The glass melted separately has a grain size D_{50} ranging between 0.7 and 7μm when being added to the ground material, whose grain size is similar or larger.

[00029] Therefore the present invention also relates to a glass used as a sintering aid for resorbable materials containing calcium phosphates with the exception of tri-calcium phosphate, which glass is characterized by the following chemical composition in % by weight:

SiO_2:	68-78,	preferably 73-78,	particularly 74-75
MgO:	5-12,	preferably 8-11,	particularly 8.5-10
Na_2O:	12-27,	preferably 12-19,	particularly 14.5-17
K_2O:	0-22,	preferably 0-5	
P_2O_5:	0-20,	preferably 0-10.	

[00030] Another processing option consists in grinding the material, adding commonly used sintering aids and processing the slurry obtained in this way into a sheet which has an open-pore structure once the firing process is finished.

[00031] Advantageously, the material according to the invention can also be provided in combination with a metallic implant surface. The material's coefficient of expansion ranges between 12 and 18 x 10^{-6} K^{-1}, measured using a dilatometer (silica

glass pushrod dilatometer (*Kieselglas-Schubstangen-Dilatometer*) manufactured by Netzsch Gerätebau GmbH, Germany), so that an adaption to known steels, e.g. chromium-cobalt-molybdenum steels having similar coefficients of expansion, is particular advantageous.

[00032] The present invention also relates to the use of the X-ray amorphous-crystalline material according to the invention for manufacturing granulated materials, ceramic bodies or ceramic sheets.

[00033] The invention will hereinafter be explained by means of examples. All percentages are by weight unless indicated otherwise.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1: shows ^{31}P-MAS-NMR spectra of the materials GA 1, GA 2 and GA 3 according to the invention, whose composition corresponds to Example 1 and whose phases correspond to Example 5 (MAS = Magic Angle Spinning);

Fig. 2: shows the ^{31}P-MAS-NMR spectra of the materials GA 4 and GA 5 according to the invention, whose composition corresponds to Example 2 and whose phases correspond to Example 5.

DETAILED DESCRIPTION OF THE INVENTION

Example 1

[00034] The following materials were synthesized according to the amounts indicated in the table in % by weight:

Code	CaO	MgO	P_2O_5	Na_2O	K_2O	SiO_2
GA 1	30.67	2.45	43.14	9.42	14.32	0.00
GA 2	29.92	2.39	44.53	9.19	13.97	0.00
GA 3	29.21	2.33	45.85	8.97	13.64	0.00

[00035] To facilitate understanding, this melting process can also be described as follows: GA 1; GA 2 (= GA 1 + 2,5% P_2O_5); GA 3 (= GA 1 + 5% P_2O_5).

[00036] The mixtures to be melted were weighed in as follows:

Code	$CaCO_3$ In g	MgO in g	85% H_3PO_4 in ml	Na_2CO_3 in g	K_2CO_3 in g	SiO_2 in g
GA 1	54.4	2.45	41.48	16.11	21.01	0
GA 2	53.40	2.39	42.82	15.72	20.50	0
GA 3	52.13	2.33	44.09	15.34	20.01	0

[00037] First, the components comprising calcium, magnesium, sodium and potassium and optionally silicon, are weighed in. Once the weighing-in process is finished, each mixture is mixed in a tumbling mixer for one hour. Then the 85% ortho-phosphoric acid is added to the mixture, the mixture is thoroughly ground in a mortar, stirred and dried at 100°C for one hour, ground in a mortar again and stored once more in a drying chamber at 100°C for one hour. Subsequently, the mixture was once again ground in a mortar, filled into a Pt/Rh crucible and heated up to 400°C, at which temperature it was held for one hour, then heated up to 800°C, at which temperature it was again held for one hour, and then heated up to 1,000°C, at which temperature it

was also held for one hour. The sinter cake produced in this way was cooled in air and ground in a mortar again in order to make it more homogeneous. The pretreated mixture was then filled into a platinum crucible and heated up to 1,600°C in a melting furnace. Once the aforesaid temperature had been reached, the melt was maintained at this temperature for half an hour. The low-viscosity, homogeneous melts were then poured onto a steel plate and pressed using a second steel plate so that a salt-like solidified plate was obtained. The crystallization taking place during this stage gives an opaque, white colour to the bodies obtained by the melting process.

Example 2

[00038] Following the same production procedure as described in Example 1, i.e. preparing a mixture of calcium carbonate, sodium carbonate, potassium carbonate and orthophosphoric acid, the following compositions were synthesized according to the amounts indicated in the table in % by weight:

Code	CaO	MgO	P_2O_5	Na_2O	K_2O	SiO_2
GA 4	31.54	1.19	42.37	9.17	13.95	1.78
GA 5	30.79	1.16	43.74	8.95	13.62	1.73

[00039] Low-viscosity melts were obtained for all compositions, which melts spontaneously crystallized when being cooled. The crystallization products had a white colour.

Example 3

[00040] Another manufacturing option consists, inter alia, in that the amount of phosphorus or phosphate may be brought in by means of a calcium carrier, either in its entirety or, as in the present example, in part. The following composition was synthesized according to the amounts indicated in the table in % by weight:

Code	CaO	MgO	P_2O_5	Na_2O	K_2O	SiO_2
GA 1	30.67	2.45	43.14	9.42	14.32	0.00

The mixture to be melted was weighed in as follows:

Code	$CaCO_3$ in g	Magnesium hydroxide carbonate in g	85% H_3PO_4 in ml	Na_2CO_3 in g	K_2CO_3 in g	$CaHPO_4$ in g
GA 1	0.00	5.13	4.25	16.11	21.00	74.43

[00041] The mixture to be melted was weighed in according to the amounts indicated above, mixed in a tumbling mixer for one hour, phosphoric acid was added, the mixture was dried at 100°C for one hour, cooled in air and ground in a mortar. The mixture obtained in this way was filled into a platinum crucible, placed in a furnace which had been preheated to 450°C and held at this temperature for 6 hours, and was then placed in a furnace which had been preheated to 800°C and held at this temperature for 16 hours. The crucible was taken out and the furnace was preheated to 950°C. The crucible was then held in the furnace preheated to 950°C for 6 hours. Subsequently, the sample was heated up to 1,600°C and held at this temperature for half an hour. The low-viscosity, homogeneous melt was then poured onto a steel plate and pressed using a second steel plate so that a salt-like solidified plate was obtained. The crystallization taking place during this stage gives an opaque, white colour to the bodies obtained by the melting process. A discoloration can be observed, depending upon the $CaHPO_4$ component used and undesirable amounts of iron and/or manganese contained therein.

[00042] It is also possible to directly quench the melt in a water bath once the melting process (1,600°C, 0.5h) is finished (fritting) in order to facilitate the further comminution of the product obtained by the melting process if it is to be further processed in the form of a slurry.

Example 4

[00043] The samples according to Example 1 and selected samples according to Example 2 (see the following table) were used to produce granulated materials having a grain size ranging between 315μm and 400μm in order to determine solubility. The solvent used was 0.2M TRIS-HCl buffer solution with a pH value of 7.4 and at a temperature of 37°C. The analyzed amount was 50mg using 40ml solvent. The granulated materials were stored at 37°C for a period of 120h. Subsequently, the total solubility was determined by determining the individual ions (of Ca, Mg, P, Na, K) in the solution by means of an ICP measurement:

Code	Solubility [μg/mg]
GA 1	95±8
GA 2	134±16
GA 3	221±22
GA 4	90±8
GA 5	152±10

Example 5

[00044] ^{31}P-MAS-NMR spectra of the samples according to Example 1 and Example 2 were recorded with a waiting time of 120s between the individual pulses. The samples rotated at a speed of 12.5kHz.

[00045] The quantitative composition of the samples as regards their phosphate content is indicated in the following table:

Code	Orthophosphate content $[(PO_4)^{3-}]$ in %	Diphosphate content $[(P_2O_7)^{2-}]$ in %	Chain phosphate content [predominantly $(PO_3)^{1-}$ in %
GA 1	99.5-96	0.5-4	-
GA 2	88	12	-
GA 3	79	21	-
GA 4	95	5	-
GA 5	89	11	-

[00046] The range indicated for the composition GA 1 is based on the analysis of three batches one of which was synthesized according to the manufacturing method described in Example 3, whereas only one sample was analysed for each of the other compositions.

Example 6

[00047] In the zirconium oxide bowl (250ml) of a planetary mill, the product obtained by the melting process having a composition according to code GA 1 was ground two times for 20min. The result is shown in the following table.

Code	D_{50} value [in µm]
GA 1	6.50

Example 7

[00048] The ground GA 1 sample according to Example 6 is to be processed into "scaffolds". For this purpose, a slurry was produced by combining 100g of the ground material with 45g of a mixture consisting of 90% polyethylene glycol and 10% of a commercially available surface-active agent and adding 5ml isopropyl alcohol. The slurry obtained in this way is applied onto open-pore PUR sponges (PUR = polyurethane) whose porosity ranges between 80 and 20ppi (pores per inch) by repeatedly immersing and squeezing the sponges, dried overnight in a drying chamber at 120°C and then slowly heated up to 1,000°C at a rate of 10°C per minute. The result is a spongiosa-like material the structure of which resembles that of the sponge used, while the PUR sponge has burnt completely.

Example 8

[00049] In order to further increase the strength of the spongiosa-like bodies, 3% by weight of a previously produced glass having a chemical composition of (in % by weight) 74.97 SiO_2, 9.22 MgO and 15.81 Na_2O (melted as 27.04 Na_2CO_3) and a D_{50} value of 6.56μm was added to the ground material according to GA 1 as a sintering aid. Then a slurry was produced by combining 100g of this powder mixture with 45g of a mixture consisting of 90% polyethylene glycol and 10% of a commercially available surface-active agent and adding 5ml isopropyl alcohol. The slurry obtained in this way is applied onto open-pore PUR sponges whose porosity ranges between 80 and 20ppi (pores per inch) by repeatedly immersing and squeezing the sponges, dried overnight in a drying chamber at 120°C and then slowly heated up to 1,000°C at a rate of 10°C per minute. The result is a spongiosa-like material the structure of which resembles that of the sponge used, while the PUR sponge has burnt completely.

Example 9

[00050] Samples according to Example 1 and Example 2 were produced and analyzed by means of ^{31}P-NMR measurements. The ^{31}P-MAS-NMR spectra were recorded with a waiting time of 120s between the individual pulses. The samples rotated at a speed of 12.5kHz.

[00051] As a result, it can be shown that in the case of the samples GA 1 through GA 3 (cf. Fig. 1), whose only chemical difference consists in the increasing phosphate content, this increased phosphate content is reflected in an X-ray amorphous-crystalline diphosphate content in the product obtained by the melting process, which also dramatically influenced solubility (cf. Example 4). This applies analogously to the samples GA 4 and GA 5 (cf. Fig. 2).

[00052] In the spectra shown in Fig. 1 and Fig. 2, the left (broader) peaks indicate the Q_0-groups and the right (narrower) peaks the Q_1-groups.

<u>Example 10</u>

[00053] Material composed according to code GA 1 was freshly ground, 1g of a grain size fraction <45μm was added into 100ml E-pure water, and the pH value was determined after 1min and after 72h. The result was 10.55 after one minute and 8.71 after 72 hours, i.e. a clear change towards physiological conditions could be observed.

<u>Example 11</u>

[00054] In order to enhance this effect a priori, the following experiment was carried out: A spongiosa-like body was produced according to Example 7, i.e. the composition according to code GA 1 was applied onto a PUR sponge and sintered, except that the sponge used in the present example had a porosity of 30ppi.

[00055] The moulded body obtained in this way, whose outer dimensions were approx. 11mm x 11mm x 7mm, was immersed in 100ml E-pure water and the pH value was measured after 10min. The measured value was 9.62.

[00056] Subsequently, the moulded body was eluted in E-pure water at 60°C and a pressure of 3 bars for one hour. The moulded body was then rinsed 5 times in 20ml fresh E-pure water, immersed in 100ml E-pure water again, and a pH value of 8.83 was measured after 1 hour.

[00057] This demonstrates that the pretreatment of spongiosa-like bodies described above is a useful activity as products pretreated in this way have a lower basicity, which can be advantageous both for implantation in vivo and for tissue engineering ex vivo or in vitro.

Example 12

[00058] An important feature with regard to the coating of materials with the resorbable materials according to the invention consists in that the thermal coefficient of expansion can be varied, bearing in mind e.g. that this coefficient is approx. $8 \circ 10^{-6}$ K^{-1} for titanium implants and approx. $14\text{-}16 \circ 10^{-6}$ K^{-1} for Co-Cr-Mo steels (depending upon the constituents of the alloy). In order to obtain a composite material which is optimally suited to its intended use, the temperature range in which the material is applied onto the metallic substrate must be carefully selected as in this way the substrate can be subjected to compressive strain, i.e. to preheating, in a targeted manner during the coating process thus obtaining a composite material which in general is regarded as mechanically more stable.

[00059] The following table shows some of the possible variations:

Sample	$CE_{30\text{-}100}$ (10^{-6} K^{-1})	$CE_{RT\text{--}400}$ (10^{-6} K^{-1})	$CE_{50\text{-}400}$ (10^{-6} K^{-1})
GA 1	12.15	14.84	15.14
GA 2	13.64	17.16	17.54
GA 3	13.21	16.99	17.45
GA 4	12.51	15.85	16.20
GA 5	13.29	16.69	17.08

[00060] In the table, $CE_{30\text{-}100}$ is the coefficient of expansion between 30 and 100°C, $CE_{RT\text{--}400}$ is the coefficient of expansion between room temperature (25) and 400°C, and and $AK_{50\text{-}400}$ is the coefficient of expansion between 50 and 400°C.